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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/419,517	10/18/99	KAESEMEYER W	97-092-US-C2

EXAMINER	
KIM, J	
ART UNIT	**PAPER NUMBER**
1617	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/419,517	KAESEMEYER, WAYNE H.	
	Examiner	Art Unit	
	Jennifer M Kim	1617	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,12,13 and 16-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,12,13 and 16-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Applicant's response with respect to claims 1-6, 12, 13, and 16-26 have been considered and are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 12, 13, 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGovern et al.(U.S. Patent No. 5,634,895) and Igo et al.(U.S.Patent No. 5,634,895).

3. McGovern et al. on the abstract, teaches a method for preventing onset of restenosis after angioplasty employing a HMG-CoA reductase, pravastatin.

4. McGovern et al. on column 1, lines 26-40, reports that lovastatin, a HMG-CoA reductase inhibitor reduces restenosis following angioplsty.

5. Igo et al. teaches on the abstract, column 6, lines 41-44, column 7, lines 7-12, a method of treating angioplasty restenosis and **coronary blood vessels** by administering nitric oxide donor agent including L-arginine.

6. The claims differ from the cited references in claiming combination of L-arginine, and HMG-CoA reductase inhibitor, to treat a condition such as restenosis following angioplasty. To employ combinations of L-arginine and HMG-CoA reductase inhibitor to treat a condition such as restenosis following angioplasty would have been obvious because all the components are well known individually for treating restenosis following angioplasty. It would be expected that the combination of components would treat restenosis following angioplasty as well. The motivation for combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)).

7. The therapeutic amounts of active agents to be used set forth in claim 6 and formulate prior to administration or mixed together in vivo set forth in claim 5, the route of administration set forth in claim 2, and setting a periodic indicator set forth in claim 19 are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional route of administration.

Claims 1,2,5,12, 13, 20, 21, and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al.(1994), Pharmacol. Res. (1996)(U) and Bocan (U.S.Patent No.6,093,719).

8. Wang et al. teaches on the abstract, that the dietary L-arginine prevents **atherogenesis** in the coronary artery of the hypercholesterolemic rabbit.

9. The U reference teaches that cerivastatin interferes major process involved in **atherogenesis.**

10. Bocan on the abstract teaches atorvastatin alone resulting in a less **atherogenic** lipoprotein profile.

11. The claims differ from the cited references in claiming combination of L-arginine, and HMG-CoA reductase inhibitor, cerivastatin or atorvastatin to treat a condition such as atherogenesis. To employ combinations of L-arginine and cerivastatin or atorvastatin to treat a condition such as atherogenesis would have been obvious because all the components are well known individually for treating atherogenesis. It would be expected that the combination of components would treat atherogenesis as well. The motivation for combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)).

Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacAllister et al.(1996)(V).

12. The (V) reference teaches that in human, **cardiovascular disease** such as **hypertension** is resulted from abnormalities of the L-arginine:NO pathway accelerates **atherogenesis** within the **cardiovascular system.**

See also paragraphs 5, 9 and 10 above.

The difference between above references and Applicant's claiming invention is employing combination of L-arginine and HMG-CoA reductase inhibitors to treat other heart and vascular related diseases set forth in claim 3.

13. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to employ combination of L-arginine and HMG-CoA inductase inhibitors to treat other heart and vascular related diseases since all of the above reference relates to treating disease relating to cardiovascular and coronary blood vessels caused by atherogenesis. One having ordinary skill in the art would have been motivated to combine both active agents to treat other disease condition set forth in claim 3 with reasonable expectation of success since each of active agents are useful treating diseases relating to **cardiovascular** and **coronary blood vessels** caused by **atherogenesis.**

With regard to claim 19, Lefer et al.(1993), teaches HMG-CoA reductase inhibitor and L-arginine markedly attenuated both

reduced basal NO production and the increased adhesiveness of the endothelium when basal release NO in rabbit was blocked with L-NAME.

14. The claims differ from the cited references in claiming combination of L-arginine, and HMG-CoA reductase inhibitor, to stimulating NO synthase. The claims are drawn to a mechanism of action inherent in the effect in treating the claimed disease with the individual claimed active agent. To employ combinations of L-arginine and HMG-CoA reductase inhibitor to stimulate NO synthase would have been inherent because each of the components are well known individually for attenuating effect of L-NAME in rabbit. Accordingly, Applicant's a claiming mechanism of stimulating NO synthase was achieved individually when both agents markedly attenuated effect of L-NAME (reducing basal NO production and the increased adhesiveness of the endothelium). Therefore, it would be expected that the combination of each active agent would achieve same effect as well.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under,35 U.S.C. 103.

None of the claims are allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer

Kim whose telephone number is (703) 308-2232. The examiner can normally be reached on Monday through Friday from 9 AM. to 4 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, can be reached on (703) 308-4612. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Theodore J. Criares
Primary Examiner
Art Unit 1617

jmk
April 13, 2001